Jusmeen Sarkar DVM, MS, DACVAA, CVA
ISVMA 2023 Proceedings

Sedatives, Tranquilizers and Anxiolytic Drugs in Cats and Dogs

- Opioids
    - Pure mu agonists most analgesia
    - Kappa agonists more sedation, mild analgesia
- Benzodiazepine agonists
    - Muscle relaxation, minor tranquilizer, NO analgesia
- Alpha 2 agonist
    - Sedation, muscle relaxation, analgesia
- Acepromazine
    - Major tranquilizer, muscle relaxation, NO analgesia
- Opioid or opioid + benzodiazepine or alpha 2 agonist or acepromazine
- Can consider adding ketamine 1 to 1.5 mg/kg IV
    - Do not just use opioid and ketamine – no muscle relaxation and not pleasant
- Opioids
    - Mechanism of action
        - Inhibit transmission of pain in dorsal horn
        - Inhibit somatosensory afferents at supraspinal levels
        - Decrease in release of neurotransmitters
        - Activation of descending inhibitory pathways
    - Morphine: reliable sedation; nausea; 0.5 to 1 mg/kg IM/SQ; SLOW IV
    - Hydromorphone: sometimes sedates; causes panting; 0.05 to 0.1 mg/kg IV/IM/SQ
    - Buprenorphine: no to very little sedation; difficult to reverse; 0.01 to 0.02 mg/kg IV/SQ
    - Butorphanol: decent sedation but poor analgesia; 0.2 to 0.4 mg/kg IV/IM/SQ
    - Methadone: moderate analgesia, similar potency to morphine, less nausea; 0.2 to 0.3 mg/kg IV
    - Fentanyl :3- 5mcg/kg bolus IV will last for about 20 mins; unreliable sedation as sole agent in healthy patients and cats
- Benzodiazepine agonists
    - Desired effects: muscle relaxation, anticonvulsant
    - Mechanism of action: modulate neurotransmission via GABA
    - Metabolism: hepatic; Duration of effect: 30 – 60 minutes
    - Diazepam: 0.1-0.3 mg/kg IV
    - Midazolam: 0.1-0.3 mg/kg IV/IM
    - Side effects
        - Minimal changes in CV function but can cause decrease in HR if tachycardia is from stress
        - Excitement, dysphoria, aggression
    - Contraindications

- Known or suspected PSS
- Signs of hepatic encephalopathy, hepatic failure
- Unreliable sedation; not useful as sole agent

- Alpha 2 agonist: dexmedetomidine
  - Desired effects: muscle relaxation, sedation, analgesia
  - Metabolism: hepatic; Duration of effect: (s) 25 to 45 minutes; (a) 1 hour (published doses) – we use much lower doses
  - Side effects
    - Cardiovascular
      - *Phase 1 – vasoconstriction, increase BP, reflex bradycardia*
      - *Phase 2 – decreased sympathetic tone, HR and BP*
      - *HR and cardiac index decrease by 50-60% in conscious cats and dogs*
    - GI - vomiting
    - Endocrine - hyperglycemia
    - Thermoregulation - altered ability to maintain temperature and hypothermia
  - Dexmedetomidine: caution
    - Cardiovascular disease
    - Central nervous system disease
    - Hepatic or renal disease
    - Upper airway disease
  - Dose Range
    - Dogs: 2 to 4 mcg/kg IV; 3 to 5 mcg/kg IM
    - Cats: 3 to 5 mcg/kg IV, 5 to 10 mcg/kg IM
    - I tend to use lower dose range IM and combine with ketamine if patient will need higher dose so that we don't cause intense vasoconstriction and then have difficulty with venipuncture or IV catheter placement
    - Use lowest dose in critical patients

- Zenalpha (Dechra)
  - Combination of medetomidine and vatinoxan
    - Medetomidine: alpha 2 agonist resulting in sedation, analgesia, muscle relaxation
      - Dose dependent vasoconstriction, hypertension and reflex bradycardia
    - Vatinaxan: peripheral alpha 2 antagonist that blocks the peripheral effects of medetomidine
      - Less of the vasoconstriction, hypertension and reflex bradycardia
  - NOT FOR USE IN CATS
  - FOR IM USE IN DOGS ONLY
  - Labeled for procedural sedation
  - Not intended for use as a premedication given its cardiovascular depression and limited duration of effect
  - Due to the pharmacokinetics of vatinoxan, the onset of effect of Zenalpha is faster than dexmedetomidine (IM)
  - Spontaneous recovery from sedation usually occurs within 30 to 40 minutes
  - Dogs should be allowed to rest quietly and not be disturbed for 5 to 15 minutes after administration of Zenalpha

- Dosing: dosing chart is provided with bottle
- If sedation is not sufficient after at least 15 to 20 minutes has elapsed, or if sedation is wearing off before the procedure has been completed, an additional dose can be administered IM at half of the original dose
- Some degree of increased blood pressure and bradycardia will occur, but it is not as much as we see with dexmedetomidine
- Dogs that cannot handle an alpha 2 agonist should not receive Zenalpha
- It is prudent to start with a half dose and see how the dog does
- If combined with butorphanol, hydromorphone or midazolam, the duration of sedation can be expected to be prolonged
- As with all alpha 2 agonists or any drug combination that causes moderate to heavy sedation, flow by oxygen should be provided and monitoring and record keeping must be performed
- If reversal is required, atipamezole at 50% of the Zenalpha volume is administered IM
- My experience using Zenalpha will be presented at the convention

- Acepromazine
  - Desired effects: anxiolytic, muscle relaxation, antiemetic, antiarrhythmic
  - Mechanism of action: blockade of dopamine receptors in basal ganglia and limbic system
  - Metabolism: hepatic; Duration of effect: several hours
  - Dose: 0.003-0.01mg/kg IV; 0.01 to 0.02mg/kg IM
  - Side effects
    - Vasodilation
    - Decreased CO
    - Decreased Hct
    - Inhibition of platelet aggregation
    - Hypothermia
  - Contraindications: hypovolemia, hypotension, anemia, bleeding disorders, liver disease

- Monitoring sedation
  - Level of sedation
  - Control of airway/oropharynx
  - Heart rate
  - Respiratory rate
  - Blood pressure
  - Temperature
  - SpO2
    - Provide flow by O2 to keep SpO2 > 94%
- Recovery
  - Return to pre-sedation state
  - Not mentally ‘normal’ for several hours
  - May have residual weakness
  - Reversal
    - Naloxone – 0.04mg/kg is full dose for reversal
      - Easy way to calculate this is the weight in pounds divided by 10
      - For a 10 pound cat, the full reversal dose of naloxone is 1cc

        - Unless arrest situation, I usually start with a ¼ to 1/3 reversal to reverse sedation but not reverse analgesia
    - Atipamezole (Antisedan)
        - Reverse sedation (and analgesia) from alpha 2 agonists (dexmedetomidine, medetomidine and Zenalpha)
        - Given IM unless arrest situation
        - Actual dosage is based on mcg/m2 but because of the concentration, the reversal ends up being the same volume as the alpha 2 agonist
    - Flumazenil
        - Reverse dysphoria from agonists
        - Reverse dysphoria/stupor from endogenous compounds
        - Caution if predisposed to seizures
        - 0.01 mg/kg is full dose for reversal
        - Easy way to calculate this is the weight in pounds divided by 10
        - For a 20 pound dog, the full reversal dose of flumazenil is 2 cc
        - Unless arrest situation, I usually start with a ¼ to 1/3 reversal to reverse sedation but not reverse all of the anxiolysis
- Oral drugs for anxiolysis and to enhance sedation
    - Pros
        - Can often times facilitate examination, blood draws, non-painful diagnostic procedures without injectable drugs
        - Very inexpensive
        - Cardiovascular and respiratory parameters are usually well maintained
        - Level of sedation is usually mild if at all present
        - Allows for use of low doses of injectable sedatives
            - Potential for fewer side effects and decreased overall cost
    - Cons
        - Patient must be able to be medicated orally
        - Onset of efficacy is at least 30 to 45 minutes
        - Residual effects can last for hours, even into the next day especially in geriatric patients and patients with renal disease (gabapentin)
        - No reversal exists
    - Gabapentin
        - Dogs 10 to 20 mg/kg
        - Cats 15 to 30 mg/kg
        - Use a lower dose in patients with kidney disease
        - My preference is to combine with trazodone to minimize the duration of the residual effects
    - Trazodone
        - Dogs 4-5mg/kg
        - Cats 7-10mg/kg
- Combining drugs (oral or injectable) when patient is on behavior modifying medications
    - Importance of getting updated medication list
    - Patients with moderate to severe anxiety should continue to receive their behavior-modifying medications even on the day of the appointment
    - The risk of serotonin syndrome can increase when combining any of the following

        - Trazodone, antihypertensive drugs, aspirin, azole antifungals, cisapride, CNS depressants, digoxin, diuretics, fluoroquinolones, macrolide antibiotics, monoamine oxidase inhibitors (selegiline), metoclopramide, NSAIDs, ondansetron, phenothiazines, SSRI antidepressants (fluoxetine, sertraline, paroxetine), tricyclic antidepressants (amitriptyline), and tramadol.
    - Signs of serotonin syndrome can include vomiting, diarrhea, seizures, hyperthermia, sensitivity of the skin, depression, dilation of pupils, vocalization, blindness, excessive salivation, difficulty breathing, loss of control of movements, paralysis, disorientation, coma, and death.

CASE Examples will be presented at the conference